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Abstract

Objectives: To estimate the prevalence and determine the factors associated with the use of antibiotics in the management of non-bloody diarrhoea in children under 5 years of age in Sub-Saharan Africa (SSA).

Methods: We conducted a meta-analysis of demographic and health survey datasets from 30 countries in SSA. Pooled prevalence estimates were calculated using random effects model. Chi-square tests were employed to determine the factors associated with antibiotic use.

Results: The pooled prevalence of antibiotic use among cases of non-bloody diarrhoea in children under 5 years of age was 23.1% (95% CI 19.5 – 26.7). The use of antibiotics in children with non-bloody diarrhoea in SSA was associated with ($p < 0.05$) the source of care, place of residence, wealth index, maternal education and breast feeding status.

Conclusion: We found an unacceptably high use of antibiotics to treat episodes of non-bloody diarrhoea in children under the age of 5 in SSA.

What is known about this topic?

- The appropriate treatment of diarrhoea is simple, yet it remains a problem in many low and middle income countries.
- Most cases of non-bloody diarrhoea in children are self-limiting and are caused by microorganisms which are not susceptible to antibiotic therapy
- Use of antibiotics to treat non-bloody diarrhoea in children increases the risk of adverse effects and the development of resistant bacteria.

What this study adds?

- We utilised nationally representative data to estimate the prevalence of antibiotic use in episodes of non-bloody diarrhoea in children under the age of 5 in SSA.
- We found over one-in-five cases of non-bloody diarrhoea were treated with antibiotics in SSA
- We highlight the need to educate prescribers and parents in SSA on appropriate management of diarrhoea and the consequences of inappropriate use of antibiotics in children.

Introduction

Diarrhoea is one of the leading cause of morbidity and mortality in children under five years old worldwide with about 1.7 billion episodes and 578,000 deaths every year.[1] Most of these episodes and deaths occur among children in Africa with about 440 million cases and 350,000 deaths annually.[2]

The appropriate treatment of diarrhoea is simple, yet it remains a problem in many low and middle income countries (LMICs). Recent reviews of diarrhoea management in children in LMICs have revealed a high degree of inappropriate practise including excessive fluid curtailment and antibiotic prescribing.[3-5] The existing WHO guideline recommends the use of oral rehydration solution (or an intravenous electrolyte solution in cases of severe dehydration) as well as zinc supplementation and continued feeding for the treatment and management of diarrhoea in children.[6] The guideline only recommends the use of antibiotics in cases of bloody diarrhoea, suspected cholera or associated sepsis.

The inappropriate use of antibiotics in children with diarrhoea can result in the development of antibiotic resistance. In addition, the majority of antibiotics can increase the risk of diarrhoea because of their effect on gut microflora.[7] Very few studies have focussed on understanding the extent of antibiotic use in episodes of non-bloody diarrhoea in children in SSA. Rogawski et al.[8] reported that 48.2% and 21.5% of cases of non-bloody diarrhoea in Haydom in Tanzania and Venda in South Africa, respectively were treated with antibiotics. Also, Opondo et al.[9] found that 64.5% of cases of non-bloody diarrhoea in children were treated inappropriately with antibiotics in eight district hospitals in Kenya. However, these studies were not nationally representative and did not explore the factors associated with the use of antibiotics in children with non-bloody diarrhoea. We conducted a meta-analysis of demographic and health survey (DHS) datasets from 30 countries in SSA to determine the prevalence and factors associated with the use of antibiotics in children with non-bloody diarrhoea.

Methods

Data source

We conducted a meta-analysis of DHS data on the treatment of non-bloody diarrhoea with antibiotics in children under the age of 5 in 30 countries in sub-Saharan Africa. DHS are nationally-representative household surveys conducted by ICF Macro/MEASURE DHS on behalf of national ministries of health with financial support from many international partners including the United States Agency for International Development.[10] The standard DHS uses identical methodology including the probability sampling strategy and survey instrument to collect data that are comparable across countries.

Our study only included country datasets that were collected from 2000 to 2016 and contained disaggregated data on the type of diarrhoea- bloody and non-bloody diarrhoea in children under the age of 5. The datasets of 38 countries in SSA were available from DHS programme website. Of these 38 datasets, 30 met the inclusion criteria. Details of the included countries are contained in Figure1.

Data analysis

All DHS datasets were downloaded with permission from the DHS programme website and the data were analysed using Stata version 14 and Microsoft Excel 2016.

The variables from the DHS datasets extracted and included in our analysis were prevalence of children with diarrhoea; type of diarrhoea, whether bloody or non-bloody; proportion of children treated/untreated; proportion of children who were treated for diarrhoea, type and sources of treatment. Other variables included were the socio-demographics characteristics of children and their households including age and sex of child, mother's educational level, wealth index of households, type and geographical location of child's residence.

We employed a random effects meta-analysis to calculate pooled prevalence estimates of the use of antibiotics in children with diarrhoea. A random effects meta-analysis was used because it allows for heterogeneity across studies. Despite the similarity of the DHS study design across countries, we expected heterogeneity due to differing population parameters including geographical distribution and socioeconomic conditions in different countries and regions of SSA. A test of heterogeneity of the DHS data obtained for the different countries showed a high level of inconsistency ($I^2 > 50\%$) thereby agreeing with our decision to use the random effects model in our analysis. Furthermore, we performed sensitivity analysis by excluding from our analysis one country data at a time and the impact of excluding the data was evaluated on the summary results. This was done to examine the effect of outliers and test the robustness of our findings.

Subgroup analyses were performed to determine whether factors such as sex, age, type of residence, wealth index, education and sources of care were associated with the use of antibiotics in children under 5 years of age in SSA. The chi-square tests for association, or where appropriate for trend were calculated and results were considered statistically significant at $p < 0.05$.

Results

The datasets from the 30 countries covered 287,624 children under 5 years of age. Overall, the pooled prevalence of all types of diarrhoea was 15.7% (95% CI 14.0 – 17.4) while the prevalence estimate for non-bloody diarrhoea was 12.8% (95% CI: 11.4 – 14.2). The majority of the cases of non-bloody diarrhoea were attended to in government health centres (17.6%), government hospitals (8.9%), government health posts or dispensaries (7.4%), shops (6.6%), community pharmacies (4.0%) and private hospitals/clinics (3.8%).

The pooled prevalence of antibiotic use among cases of non-bloody diarrhoea in children under 5 years of age was 23.1% (95% CI 19.5 – 26.7). Antibiotics were commonly used among cases of non-bloody diarrhoea in Congo-Brazzaville 58.6% (95% CI 55.9 – 61.3) and Sierra Leone 47.1% (95% CI 43.9 – 50.3) (Figure 1). The regional estimate was lowest in east Africa 18.7% (95% CI 13.9 – 23.6) and highest in central Africa 27.6% (95% CI 16.9 – 38.3). The higher estimate in central Africa was due to the contribution of Congo-Brazzaville. The sensitivity analysis conducted by excluding the Congo-Brazzaville data yielded a pooled estimate of 21.8% in the central region, which is comparable to southern African region. The SSA pooled estimate obtained following the sensitivity analysis (21.9%, 95% CI 18.8 – 24.9) was comparable to our previous estimate.

Table 1 summarises data based on the sub-group analyses performed. The subgroup analyses suggested that the use of antibiotics in children with non-bloody diarrhoea in SSA was significantly associated with ($p < 0.05$) the source of care, type of residence, wealth index, maternal education and breast feeding status. The results revealed that antibiotics were commonly used in children who sought advice or treatment from private hospitals/clinic and community pharmacies with pooled estimates of 41.1% (95% CI 34.1 – 47.4) and 41.8% (95% CI 34.8 – 48.9), respectively.

Discussion

The main contributions of our study lie in the use of nationally-representative data, the comprehensiveness of the factors explored and the application of meta-analysis to provide pooled estimates on the prevalence of antibiotic use in episodes of non-bloody diarrhoea in children under the age of 5 in SSA. We found a high use of antibiotics to treat episodes of non-bloody diarrhoea in children under the age of 5 in SSA: over one-in-five cases of non-bloody diarrhoea were treated with antibiotics. Most cases of non-bloody diarrhoea in children are self-limiting and caused by microorganisms which are not susceptible to antibiotic therapy such as rotavirus or for which the efficacy of antibiotic therapy is somewhat uncertain such as in campylobacter infections.[9,11] Up to 13% of cases of non-bloody diarrhoea are due to *Shigella* spp or enteroinvasive *Escherichia coli*,[12] which may justify antibiotics in children with severe toxicity or systemic symptoms of sepsis. However the high rates of antibiotic prescribing seen in many SSA countries cannot be justified by the data on the aetiology of non-bloody diarrhoea and will only lead to antibiotic resistance and antibiotic-associated diarrhoea. Therefore, our findings underscore the need to educate both prescribers and parents in SSA on appropriate management of diarrhoea and the consequences of inappropriate use of antibiotics in children.

This study, however, is not without limitations. Some countries in SSA were not included due to non-availability of DHS data for the study period considered. Also, the data used in this study was based on self-reported data and so liable to recall and social desirability biases which may result in under-estimation of the prevalence of antibiotics used in non-bloody diarrhoea. Despite these limitations, this study provides additional insight into the management of diarrhoea in SSA and could prompt appropriate health system response.

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Competing interest

None declared

References

1. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385(9966):430-40.
2. Walker CL, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. Lancet, 2013. 381(9875):1405-1416.
3. Carvajal-Vélez L, Amouzou A, Perin J, Maïga A, Tarekegn H, Akinyemi A, et al. Diarrhea management in children under five in sub-Saharan Africa: does the source of care matter? A Countdown analysis. BMC Public Health. 2016;6(1):830.
4. Perin J, Carvajal-Velez L, Carter E, Bryce J, Newby H. Fluid curtailment during childhood diarrhea: a countdown analysis. BMC Public Health, 2015;15(1):588.
5. Diallo AF, Cong X, Henderson WA, McGrath J. Management of childhood diarrhea by healthcare professionals in low income countries: an integrative review. Int J Nurs Stud. 2017;66:82-92.
6. World Health Organization. 2005. The treatment of diarrhoea: a manual for physicians and other senior health workers. Available:

http://apps.who.int/iris/bitstream/10665/43209/1/9241593180.pdf [Accessed 02 October 2017].
7. Diniz-Santos DR, Silva LR, Silva N. Antibiotics for the empirical treatment of acute infectious diarrhea in children. Braz J Infect Dis. 2006;10(3):217-27.
8. Rogawski ET, Platts-Mills JA, Seidman JC, John S, Mahfuz M, Ulak M, et al. Use of antibiotics in children younger than two years in eight countries: a prospective cohort study. Bull World Health Organ. 2017;95(1):49-61.
9. Opondo C, Ayieko P, Ntoburi S, Wagai J, Opiyo N, Irimu G, et al. Effect of a multi-faceted quality improvement intervention on inappropriate antibiotic use in children with non-bloody diarrhoea admitted to district hospitals in Kenya. BMC Pediatr. 2011;11:109.
10. Measure DHS. Methodology: survey process. Available: http://dhsprogram.com/What-We-Do/Survey-Process.cfm [Accessed 16 May 2017].
11. O'Ryan G M, Ashkenazi-Hoffnung L, O'Ryan-Soriano MA, Ashkenazi S. Management of acute infectious diarrhea for children living in resource-limited settings. Expert Rev Anti Infect Ther. 2014;12(5):621-32.
12. Liu J, Platts-Mills JA, Juma J, Kabir F, Nkeze J, Okoi C, et al. Use of quantitative molecular diagnostic methods to identify causes of diarrhoea in children: a reanalysis of the GEMS case-control study. Lancet. 2016;388(10051):1291-301.

Table & Figure

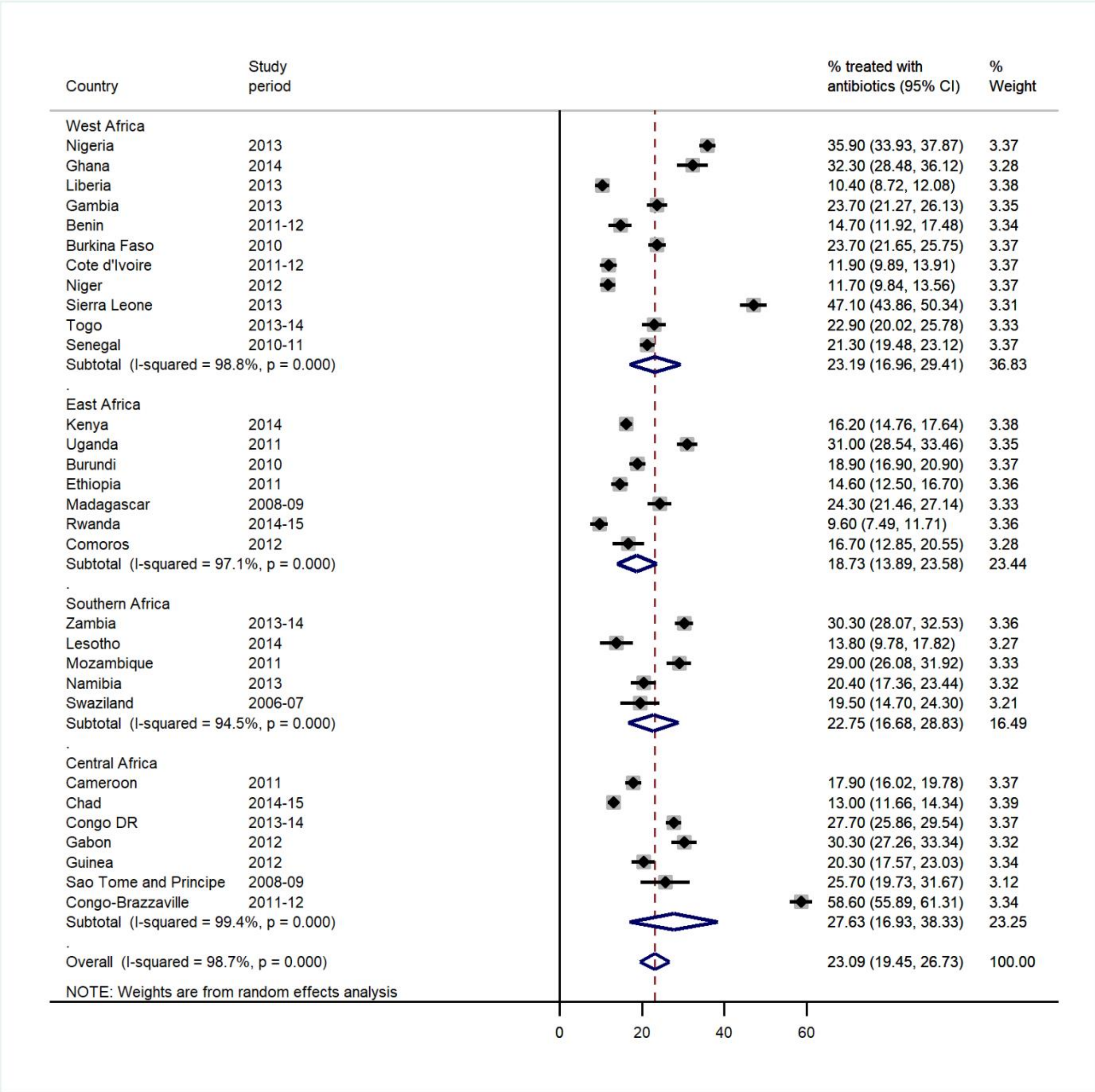

Figure 1: Meta-analysis for the prevalence of antibiotic use among cases of non-bloody diarrhoea

Table 1: Prevalence of antibiotic use in non-bloody diarrhoea by demographic category

Category	**Number of Children with non-bloody diarrhoea**	**Prevalence estimate % (95% CI)**	**Test for association or trend**
Sex of child			$X^2 = 1.778$, $p = 0.182$
Male	18268	23.5 (19.9 – 27.1)	
Female	16809	22.9 (16.2 – 39.8)	
Age of child			$X^2 = 0.018$, $p = 0.893$
0	9307	21.1 (17.6 – 24.5)	
1	11395	25.0 (21.2 – 28.8)	
2	7040	22.9 (18.9 – 26.9)	
3	4413	22.1 (18.0 – 26.2)	
4	2922	22.0 (17.8 – 26.2)	
Currently breastfeeding			$X^2 = 13.485$, $p = 0.000$
No	13160	24.1 (20.0 – 28.2)	
Yes	21917	22.4 (18.9 – 26.0)	
Type of residence			$X^2 = 109.137$, $p = 0.000$
Urban	10771	26.7 (22.5 – 31.0)	
Rural	24306	21.6 (18.2 – 25.1)	
Wealth Index*			$X^2 = 176.047$, $p = 0.000$
Poor	16596	20.7 (16.9 – 24.5)	
Middle	6789	22.0 (18.6 – 25.5)	
Rich	11668	27.6 (23.6 – 31.6)	
Mother's highest level of education*			$X^2 = 184.584$, $p = 0.000$
No education	14740	20.5 (17.2 – 23.8)	
Primary	12360	24.0 (20.4 – 27.7)	
Secondary	7352	27.9 (23.3 – 32.4)	
Higher	611	33.0 (26.1 – 39.8)	
Sources of care*			$X^2 = 3447.205$, $p = 0.000$
Government hospitals	3131	38.5 (32.3 – 44.8)	
Government health centres	6184	35.2 (29.9 – 40.4)	
Government health posts/dispensaries	2603	30.9 (24.4 – 37.5)	
Private hospitals/clinics	1347	41.1 (34.1 – 47.4)	
Community pharmacies	1391	41.8 (34.8 – 48.9)	

Shops	2321	33.6 (25.5 – 41.7)	
Market	1236	21.6 (6.9 – 36.3)	
Traditional practitioners	1011	5.0 (3.6 – 6.5)	
Others	1626	16.8 (11.8 – 21.9)	
Did not seek treatment from any provider	14189	9.3 (7.3 - 11.2)	

N=35,077 *Category with some missing data